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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,727	09/14/2005	Martin Krause	BB-124	1308

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	**PAPER NUMBER**
1652	

NOTIFICATION DATE	DELIVERY MODE
03/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/518,727	KRAUSE ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,22 and 24-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8, 22 and 24-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

With supplemental amendment, filed 11/20/09, in response the office action, mailed on 08/04/2009, the applicants amended claims 1-2, 6, 25, 31, and added new claims 39-40. Claims 1-6, 8, 22 and 24-40 are currently pending in the instant application. Claims 1-6, 8, 22 and 24-40 will be examined.

Applicants' arguments filed on 11/20/09, in response to a previous office action mailed on 08/04/2009, have been fully considered but they are found unpersuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections 35 U.S.C 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-6, 8, 22 and 24-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's amendment of claims 1 and 6 necessitated these rejections.

Claim 1 is indefinite because of the following reasons: Claim 1b recites "A constitutes ...Y is a group--- PRG -----labeled." It is unclear what "A", "Y" and "PRG" are referred to. There is no antecedent basis for A, Y or PRG. For examination purposes, it will be assumed that the claim recites, "b) providing a reagent for the analysis of peptides which comprises A, Y and PRG". Correction is required.

Claim 6 is indefinite because of the following reasons: Claim 1b recites "A constitute ...Y is a group--- PRG -----."It is unclear what "A", "Y" and "PRG" are referred to. There is no antecedent basis for A, Y or PRG. For examination purposes, it will be assumed that the claim recites, "b) providing a reagent for the analysis of peptides which comprises A, Y and PRG". Correction is required.

Claim Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8, 22 and 24-38 remain rejected and new claims 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (WO 00/11208, from IDS) in view of Moutiez et al (Analyst 1997, 122, pp 1347-1352) and Li et al. (J. Am. Soc. Mass spectro. 1997, 8, pp 781-792) as explained in prior office action and stated again below:

Aebersold et al. teach a method of identification and quantification of a protein in a sample by cleaving the protein to peptides using a proteolytic enzyme (page 18, pargh. 4) and using a reagent A-L-PRG, wherein A is linked to a solid support (wherein, A comprises biotin, oligohistidine, etc, page 12) and is covalently linked to linker L (L contain metal bound chelate, page 14, 2nd parg. and may contain disulfide group, which is cleavable, page 6, last pargh.); PRG comprises a sulfhydryl group, or

an enzyme substrate (page 6, 2nd pargh.) N- hydroxysuccinimide ester groups, etc (claim 32 of Aebersold et al.) to bind to the cleaved peptides. Aebersold et al. teach the use of a tandem technique comprising electrospray ionization mass spectrometry coupled with liquid chromatography (HPLC/ESI-MS/MS (FIG 7), peptide sequence information (page 19, 2nd pargh.) combined with isotope tags for qualitative and quantitative analysis of the protein in a sample. Although Aebersold et al. teach the use of a linker L being labeled with isotopes, they do not label the proteins with said isotope. The A-L-PRG reagent of Aebersold et al (similar to applicants' A-Y-PRG) comprises a chelated metal ion and the stable isotope in their L and use the stable isotope as standard in mass spectrometric analysis. However Aebersold et al. do not use a reagent A-Y-PRG wherein said reagent is not isotopically labeled and hence does not use metal ion as a standard in mass spectrometric analysis.

Use of metal ion as a standard in mass spectrometric studies is well known in the prior art (see page 781, Li et al.). Li et al. teach a well characterized spectra of peptide bound silver ion in mass spectral analysis (Figure 1, page 783.)

It is well known in the art the advantage of purifying and detecting proteins using chelated metal tags comprising various metal ions (Porath et al Prot express and Pur. 1992, 3, 263-281, from IDS) using a variety of chelating agents, such as lanthanide metal ions with DOTA (Moutiez et al). Moutiez et al teach a Gd^{3+} ion chelated to DOTA and teach its separation using metal ion chelate affinity chromatography (page 1350 2nd column) and teach that lanthanide metal complex can be detected using luminescence technique (page 1347 2nd column 2nd paragraph).

Therefore in order to identify and quantify proteins in proteomic samples, one of ordinary skill in the art is **motivated** to modify the A-L-PRG of Aebersold et al with Gd^{3+} DOTA chelate not being modified by isotope label and use the metal ion as standard (as taught by Li et al) in the method of Aebersold et al, because a peptide sample attached to L-PRG with Gd^{3+} DOTA can be separated by metal ion chelate affinity column by HPLC, and optionally can be detected by luminescence before passing into the mass spectrometer.

As such, it would have been obvious to one of ordinary skill in the art to combine the teachings of Aebersold et al, Moutiez et al and Li et al to make an A-L-PRG regent having Gd^{3+} DOTA complex in L, use it in the method of identification and quantification of proteins in a sample by a tandem technique comprising electrospray ionization mass spectrometry coupled with liquid chromatography (HPLC/ESI-MS/MS (FIG 7), peptide sequence information using Gd metal ion as standard, and optionally detecting the Gd^{3+} DOTA attached polypeptide by using luminescence before passing the sample into the Mass spectrometer.

Arguments and response

Applicants' argue, at pages 8-12 of their amendment of 11/22/09, that none of the three references teach or suggest a method of identification and quantification of a protein in a sample using a tandem technique comprising electrospray ionization mass spectrometry coupled with liquid chromatography (HPLC/ESI-MS/MS and peptide sequence information combined with metal tags for qualitative and quantitative analysis of the protein in a sample. Applicants' arguments filed on 11/22/2009 have been fully

considered, but they found unpersuasive. If Aebersold et al were to teach a metal labeled reagent, they would anticipate applicants' invention. However as explained above other references teach the advantages of using metal ion labeled reagent. As explained above, Li et al. teach a well characterized spectra of peptide bound silver ion in mass spectral analysis. It is well known in the art the advantage of purifying and detecting proteins using chelated metal tags comprising various metal ions using a variety of chelating agents, such as lanthanide metal ions. Therefore in order to identify and quantify proteins in proteomic samples, one of ordinary skill in the art is **motivated** to modify the A-L-PRG of Aebersold et al with Gd^{3+} DOTA chelate not being modified by isotope label and use the metal ion as standard (as taught by Li et al) in the method of Aebersold et al, because a peptide sample attached to L-PRG with Gd^{3+} DOTA can be separated by metal ion chelate affinity column by HPLC, and optionally can be detected by luminescence before passing into the mass spectrometer. Thus, the claimed invention remains *prima facie* obvious over the prior art of record.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Examiner, Art Unit 1652

/Delia M. Ramirez/
Primary Examiner, Art Unit 1652